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Takayasu's Arteritis Associated With Factor V Leiden

Daniel D. Shin and John E. Godwin*

Department of Medicine, Loyola University Medical Center, Maywood, Illinois

Takayasu's arteritis (TA) is a rare, chronic, and idiopathic vasculitis of the aorta and/or its main branches. There have been case reports of this disease associated with immune hypercoaguable states, namely raised antiphospholipid antibodies. Investigations of the thrombotic nature of Takayasu's arteritis have shown elevated levels of B-thromboglobulin, platelet factor 4, thrombin-antithrombin III complex, and fibrinopeptide A. We report the first case of TA associated with the Factor V Leiden gene defect (Activated Protein C Resistance). The patient is a 30-year-old female who presented with six months of bilateral lower and upper extremity claudication, carotid artery tenderness, diminished brachial pulse and no measurable blood pressure in the left arm, an erythrocyte sedimentation rate (Westergren) of 62 mm/hr, and an angiogram meeting the clinical criteria for TA. Her symptoms showed a dramatic response to high-dose oral glucocorticosteroids and she was also maintained on long-term anticoagulation. This case illustrates that hereditary hypercoagulable states can coexist with acquired vasculitidies and that further investigation into these associations and their pathophysiologic interaction is warranted. Am. J. Hematol. 60:237–238, 1999. © 1999 Wiley-Liss, Inc.

Key words: Takayasu's arteritis; Factor V Leiden; hypercoagulable state

INTRODUCTION

Takayasu's arteritis (TA), or pulseless disease, is a systemic inflammatory disease with a chronic idiopathic vasculitis of the aorta and/or its main branches. In some instances, the disease has been reported to occur concomitantly with acquired immune hypercoagulable states, namely raised antiphospholipid antibodies [1,2]. Another report showed elevations of thrombin-antithrombin III complex (TAT), platelet factor 4 (PF4), B-thromboglobulin (BTG), and fibrinopeptide A (FPA) indicating a hypercoagulable state [3]. In this report we describe a patient with both an inherited hypercoagulable disorder, Factor V Leiden, and TA.

BRIEF REPORT

The patient is a 30-year-old Middle Eastern female who presented with six months of bilateral lower and upper extremity claudication, pain over the peripheral arteries, and erythematous skin nodules. The patient was admitted for a work-up of possible arterial thrombosis. She was found to be homozygous for Factor V Leiden, and negative for lupus anticoagulant, anticardiolipin antibodies, Protein C, S, and antithrombin. Also discovered were an erythrocyte sedimentation rate of 62 mm/hr, carotid artery tenderness, a diminished brachial pulse, and no measurable blood pressure in the left arm. She had an angiogram meeting the clinical and angiographic criteria for TA most recently described by Sharma et al. [4]. She was placed on heparin and begun on oral warfarin. Her subsequent clinical course showed improvement of her arm claudication while on high-dose oral glucocorticosteroids (prednisone 1 mg/kg/day), and methotrexate.

DISCUSSION

In this report we describe the finding of a rare arteritis with a genetic predisposition to thrombosis, Factor V Leiden mutation, in the same individual. The presence of the Factor V Leiden mutation made the pursuit of the diagnosis of TA more difficult, as the patient's initial symptoms were attributed solely to thrombosis from Factor V Leiden.

TA is a rare disease with a prevalence of 2.6 cases per

*Correspondence to: John E. Godwin, M.D., Cardinal Bernadin Cancer Center, Loyola University Medical Center, 2160 South First Avenue, Maywood, IL 60153. E-mail: jgodwin@luc.edu.

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million persons per year. First thought to be a disease of young Asian females, it has now been described throughout the world, including the Middle East [5,6], and may be underdiagnosed in North America [7]. Thrombus formation is evident in affected arteries of TA, but its significance in the disease is unknown. The thrombogenic nature of this disorder has been investigated in 30 patients with the disease and these patients were found to have significant elevations of PF4 and BTG (markers of platelet activation) and TAT and FPA (markers of thrombin generation), indicating an acquired hypercoagulable state [3]. Interestingly the authors also concluded that the hypercoagulable state of TA did not involve endothelial damage, since normal levels of von Willebrand factor antigen and thrombomodulin were present in their cases. The abnormal markers of platelet activation and thrombin generation were present in patients with clinically active and inactive disease. In contrast, other authors have reported uniformly elevated levels of anti-endothelial cell antibodies (AECA) in patients with TA compared with normal subjects [8]. But they also stated that the significance of AECA in TA pathogenesis is unknown and that the antibody may be a marker of vasculitis rather than a cause.

The finding of elevated antiphospholipid antibodies has been described in two cases of TA [1]. In another study of 34 TA patients, 41% showed elevated antiphospholipid antibodies [2]. None of the patients in either of these studies had features of primary antiphospholipid syndrome. Both authors proposed that antiphospholipid antibodies may contribute to the vasculopathy of TA. In this patient however, neither the lupus anticoagulant or anti-cardiolipin antibodies were found.

Factor V Leiden is a gene mutation resulting in the substitution of adenine for glutamine at position 506 of the factor V gene, rendering it resistant to inactivation by Protein C. Its prevalence is much higher than TA, occurring in approximately 3% of the general population [9]. It has been estimated to carry a 7-fold relative risk for venous thrombosis in persons who are heterozygous and an 80-fold relative risk for those who are homozygous [10].

Because our patient has both disorders, she carries a significant risk for venous and arterial thrombosis. How the two diseases interact pathophysiologically is unknown. The role of Factor V Leiden in promoting the vasculopathy in TA is not clear, since the hypercoagulable state of the Factor V Leiden is not antibody mediated, unlike the cases of raised antiphospholipid antibodies mentioned previously. This is the first description of the Factor V Leiden abnormality with TA. This patient requires both immunosuppressive and anti-coagulant therapies. Whether anticoagulant therapy will provide any direct benefit to her TA is unknown. Further investigation into the pathophysiologic interaction of these hypercoagulable disorders is warranted.

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